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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/799,514	SPERTINI ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-70* is/are pending in the application.

4a) Of the above claim(s) *66-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

02/16/06

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :0
7/26/2004 & 6/22/2004.

DETAILED ACTION

1. Claims 55-70 are pending.

2. Applicant's election without traverse of Group I, claims 55-65, in the reply filed on 11/16/2006 is acknowledged.

3. Claims 66-70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

4. Claims 55-65 are currently under examination as they read upon a method for generating an improved composition of contiguous overlapping peptide fragments for a selected polypeptide allergen.

5. Applicant's IDS documents filed on 06/22/2004, 07/26/2004 and 02/26/2005 are acknowledged. The International Search Report (references C13 and C14) and PCT written opinion (reference C44) were crossed out but the references listed thereon had been considered.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 55-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicant's amendment on 09/21/2005 asserts that no New Matter has been added, but Applicant does not provide support for new claims 55-65. However, the specification does not appear to provide an adequate written description for the following newly added limitations: A method for generating an improved composition of contiguous overlapping peptide fragments (COPs) for a selected polypeptide allergen comprising the steps of: (1) determining candidate contiguous overlapping peptides by a method comprising:(a) conducting a structural analysis of the selected allergen; (b) selecting one or more separation sites to provide contiguous overlapping peptide fragments greater than 30 peptides in length which are linear and which peptides overlap each separation site; and producing said candidate contiguous overlapping peptide fragments; and screening said candidate COPs by the steps of: (a) selecting COPs characterized by having a T cell stimulating activity for T cells specific for the selected polypeptide allergen which is greater than a selected minimum; and (b) selecting COPs characterized by having an IgE binding activity for IgE's reactive with the selected polypeptide allergen which is less than a selected maximum of claim 55;

wherein the COPs have relatively reduced levels of IgE binding activity but conserved T cell stimulating activities relative to the IgE binding and T cell stimulating activities of the allergen holoprotein of claim 56; wherein the peptides overlap each separation site by 10 to 15 amino acid residues of claim 57; wherein said COPs have a T cell stimulating index which is greater than 2 of claim 58; wherein said COPs are useful in inducing tolerance to said allergen of claim 59; wherein the COPs are useful in desensitization immunotherapy of claim 60; wherein the IgE binding activity is measured by immunoblotting of claim 61; wherein the immunoblot is a dot blot of claim 62; wherein the IgE binding activity is measured by skin reaction on a dermal test of claim 63; wherein the dermal test is selected from the group consisting of skin prick tests and intradermal tests of claim 64; wherein the dermal test is an immediate intradermal (ID) test wherein COPs are selected which have a wheal and flare reaction less than or equal to 5 mm at a peptide concentration of greater than 0.1 mg/ml of claim 65.

The specification does not contemplate a method for generating an improved composition of contiguous overlapping peptide fragments (COPs) for a selected polypeptide allergen of independent claim 55. Rather, the specification is directed to compositions comprising contiguous overlapping peptide fragments and the in vivo use thereof for inducing tolerance and/or desensitization to selected allergens. The recited method for generating an improved composition of contiguous overlapping peptide

fragments (COPs) for a selected polypeptide allergen has no antecedent basis within the specification, nor is any improvement to a method contemplated.

The specification provides no support for the method comprising the step of determining candidate contiguous overlapping peptides by conducting a structural analysis of the selected allergen and selecting one or more separation sites to provide contiguous overlapping peptide fragments greater than 30 peptides in length which are linear and which peptides overlap each separation site. There are no examples in the specification of structural analysis of any selected allergens nor are there any examples of selecting separation sites within an allergen for determining the design of COPs. The specification provides no guidance or support as to how the allergens used in the in vivo were designed. There is also no support for the method of producing said candidate contiguous overlapping peptide fragments that are selected for their separation sites and structural analysis characteristics. Rather, pre-determined COPs for selected allergens are provided without any information about their design and selection process.

There is also no support for the method of screening said candidate COPs by the steps of selecting COPs characterized by having a T cell stimulating activity for T cells specific for the selected polypeptide allergen which is greater than a selected minimum and by having an IgE binding activity for IgE's reactive with the selected polypeptide allergen which is less than a selected maximum. The specification does not contemplate the method of screening any COPs from any other COPs. In order to

screen COPs with predetermined characteristics of T cell stimulating activity and reduced IgE binding, then a selection process must occur whereby some COPs are determined to not possess the required characteristics. The specification simply uses COPs in vivo to induce tolerance and /or desensitization.

Dependent claims 56-65 also do not provide support in the specification. In particular, in claim 56 the recitation of wherein the COPs have relatively reduced levels of IgE binding activity but conserved T cell stimulating activities relative to the IgE binding and T cell stimulating activities of the allergen holoprotein has no support in the specification. The word 'holoprotein' is not located anywhere in the specification, so a method including a holoprotein is not supported. Further, a method including selecting COPs with reduced IgE binding and conserved T cell stimulating activity is not contemplated because all COPs used throughout the specification had these characteristics. The specification contemplates compositions comprising these pre-selected COPs and their use *in vivo* in induce desensitization and/ or tolerance. In claim 57 the recitation of wherein the peptides overlap each separation site by 10 to 15 amino acid residues has no support in the specification. On page 6, lines 26-29 and page 10, lines 3-7, the specification discloses COPs with peptides that overlap each separation site by 10-15 amino acids for *in vivo* use. The specification does not provide support for a method of generating an improved composition of COPs that includes COPs with peptides that overlap each separation site by 10-15 amino acids. The specification contemplates the composition and using the composition *in vivo*. In claim 58 the

recitation of wherein said COPs have a T cell stimulating index which is greater than 2 has no support in the specification. On page 15, lines 5-10 the specification discloses a peptide derived from a protein allergen that may have a T cell stimulation index of 2. However, the T cell stimulation index is not described with reference to a method for generating an improved composition comprising COPs. Rather, the T cell stimulation index is disclosed as measure of a T cell response elicited by cultured T cells obtained from an individual sensitive to an allergen when exposed to an allergen or protein variant thereof. The T cell stimulation index is described only with reference to the T cell response and not with any reference to implications for the generation or screening of COPs or a composition thereof. In claims 59 and 60, the recitation of wherein said COPs are useful in inducing tolerance to said allergen and wherein the COPs are useful in desensitization immunotherapy has no support in the specification as it relates to the generation of an improved composition comprising COPs. The specification discloses a method of inducing tolerance and/ or desensitization using COPs in vivo. However, there is no support for the induction of desensitization and/ or tolerance with reference to the method comprising determining, producing and screening candidate COPs as recited in independent claim 55. In claims 61-63, the recitations of wherein the IgE binding activity is measured by immunoblotting and wherein the immunoblot is a dot blot has no support in the specification as it relates to the generation of an improved composition comprising COPs. The specification discloses the method of inducing tolerance and/ or desensitization using COPs in vivo, which includes measuring IgE binding activity by immunoblotting and specifically by dot blot. However,

there is no support for the induction of desensitization and/ or tolerance using these methods with reference to the method comprising determining, producing and screening candidate COPs as recited in independent claim 55. In claims 63-65, the recitations of wherein the IgE binding activity is measured by skin reaction on a dermal test , wherein the dermal test is selected from the group consisting of skin prick tests and intradermal tests and wherein the dermal test is an immediate intradermal (ID) test wherein COPs are selected which have a wheal and flare reaction less than or equal to 5 mm at a peptide concentration of greater than 0.1 mg/ml has no support in the specification as it relates to the generation of an improved composition comprising COPs. The specification discloses the method of inducing tolerance and/ or desensitization using COPs in vivo, which includes measuring IgE binding activity by skin reaction on a dermal test and specifically skin prick tests and intradermal tests. However, there is no support for the induction of desensitization and/ or tolerance using these methods with reference to the method comprising determining, producing and screening candidate COPs as recited in independent claim 55.

The instant claims now recite limitations which were not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification or original claims, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Obviousness is not the standard for the addition new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). New Matter is a written description issue.

Applicant is required to cancel the New Matter in the response to this Office Action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

8. Claims 55-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of: A method for generating an improved composition of contiguous overlapping peptide fragments (COPs) for **a selected polypeptide allergen** comprising the steps of: (1) determining candidate contiguous overlapping peptides by a method comprising:(a) conducting a structural analysis of **the selected allergen**; (b) selecting one or more separation sites to provide contiguous overlapping peptide fragments greater than 30 peptides in length which are linear and which peptides overlap each separation site; and producing said candidate contiguous

overlapping peptide fragments; and screening said candidate COPs by the steps of: (a) selecting COPs characterized by having a T cell stimulating activity for T cells specific for the **selected polypeptide allergen** which is greater than a selected minimum; and (b) selecting COPs characterized by having an IgE binding activity for IgE's reactive with the **selected polypeptide allergen** which is less than a selected maximum of claim 55; wherein the COPs have relatively reduced levels of IgE binding activity but conserved T cell stimulating activities relative to the IgE binding and T cell stimulating activities of the allergen holoprotein of claim 56; wherein the peptides overlap each separation site by 10 to 15 amino acid residues of claim 57; wherein said COPs have a T cell stimulating index which is greater than 2 of claim 58; wherein said COPs are useful in inducing tolerance to **said allergen** of claim 59; wherein the COPs are useful in desensitization immunotherapy of claim 60; wherein the IgE binding activity is measured by immunoblotting of claim 61; wherein the immunoblot is a dot blot of claim 62; wherein the IgE binding activity is measured by skin reaction on a dermal test of claim 63; wherein the dermal test is selected from the group consisting of skin prick tests and intradermal tests of claim 64; wherein the dermal test is an immediate intradermal (ID) test wherein COPs are selected which have a wheal and flare reaction less than or equal to 5 mm at a peptide concentration of greater than 0.1 mg/ml of claim 65.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the

genus. That is, the specification provides neither a representative number of species (selected polypeptide allergens to generate contiguous overlapping peptide fragments) to describe the claimed genus, nor does it provide a description of structural features that are common to the species (allergens whose contiguous overlapping peptide fragments have the required characteristics of claim 55). The specification provides no structural description of allergens other than the allergens species specifically exemplified by SEQ ID NOs 4, 7, 10, 14 and 17; in essence, the specification simply directs those skilled in the art to go figure out for themselves which allergens can be used for generation of contiguous overlapping peptide fragments with the required characteristics of claim 55. The specification's disclosure is inadequate to describe the claimed genus of **any selected polypeptide allergen**.

Applicant has disclosed only generation of contiguous overlapping peptide fragments with greater T cell stimulating activity and less IgE binding activity than selected minimums for the allergens of SEQ ID NOs 4, 7, 10, 14 and 17. Therefore, the skilled artisan cannot envision all the contemplated allergen and contiguous overlapping peptide fragment possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35

U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. Claims 55-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide enablement for: **a method for generating an improved composition of contiguous overlapping peptide fragments (COPs) for a selected polypeptide allergen comprising the steps of: (1) determining candidate contiguous overlapping peptides by a method comprising:(a) conducting a structural analysis of the selected allergen; (b) selecting one or more separation sites to provide contiguous overlapping peptide fragments greater than 30 peptides in length which are linear and which peptides overlap each separation site; and producing said candidate contiguous overlapping peptide fragments; and screening said candidate COPs by the steps of: (a) selecting COPs characterized by having a T cell stimulating activity for T cells specific for the selected polypeptide allergen which is greater than a selected minimum; and (b) selecting COPs characterized by having an IgE binding activity for IgE's reactive with the selected polypeptide allergen which is less than a selected maximum of claim 55; wherein the COPs have relatively reduced levels of IgE binding activity but conserved T cell stimulating activities relative to the IgE binding and T cell stimulating activities of the allergen holoprotein of claim 56; wherein the peptides overlap each separation site by 10**

to 15 amino acid residues of claim 57; wherein said COPs have a T cell stimulating index which is greater than 2 of claim 58; wherein said COPs are useful in inducing tolerance to said allergen of claim 59; wherein the COPs are useful in desensitization immunotherapy of claim 60; wherein the IgE binding activity is measured by immunoblotting of claim 61; wherein the immunoblot is a dot blot of claim 62; wherein the IgE binding activity is measured by skin reaction on a dermal test of claim 63; wherein the dermal test is selected from the group consisting of skin prick tests and intradermal tests of claim 64; wherein the dermal test is an immediate intradermal (ID) test wherein COPs are selected which have a wheal and flare reaction less than or equal to 5 mm at a peptide concentration of greater than 0.1 mg/ml of claim 65.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification only discloses allergen compositions comprising COPs and the use thereof for the induction of tolerance and/or desensitization in vivo. The specification does not disclose a method for generating an improved composition comprising COPs.

The specification does not provide sufficient guidance for the recitation of conducting a structural analysis of the selected allergen in claim 55. The structures of all allergens are not known and crystallization of proteins for structure determination is unpredictable and is based upon trial and error (Kundrot et al., Reference U, PTO-892, abstract). The specification provides no guidance or working examples as to how one would conduct a structural analysis on a specific allergen, much less any allergen as currently recited. There is also no support for how the structural analysis correlates with the selection of separation sites, reduced IgE binding and increased T cell stimulating activity.

The specification does not provide sufficient enablement for the recitation of selecting one or more separation sites to provide contiguous overlapping peptide fragments greater that 30 peptides in length which are linear and which peptides overlap each separation site; and screening the COPs characterized by having an IgE binding activity of IgEs reactive with the selected polypeptide allergen which is less than a selected maximum. There is a complete lack of guidance and working examples to support these claim recitations. The art teaches that correlations between structure and IgE binding or lack thereof cannot be predicted on an a priori structural basis

(Blumenthal et al. Reference V, PTO-892, pages 37-50 and page 39 in particular). The claims recite the generation of peptide fragments of any allergen that will have reduced IgE binding, but the specification provides no guidance as to the selection of specific COPs and what factors influence selection criteria. Attwood et al. teaches that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequence and the current structure prediction methods is unreliable (Reference W, PTO-892, entire document). Therefore, the method cannot be applied universally to all allergens despite the fact that COPs have been generated from particular allergens that exhibit the requisite reduced IgE binding. The art teaches that it would require undue experimentation to select COPs with reduced IgE binding.

There is no guidance in the specification on how the COPs are capable of inducing tolerance and/or desensitization. The state of the art is highly unpredictable with regard to successful strategies to induce allergen-specific tolerance. Larche et al. teaches that the art of allergen-specific immunotherapy is highly unpredictable (Reference X, PTO-892). Though the art is hopeful that antigen-specific immunotherapy techniques will be increasingly successful in treating and preventing allergies in the future, the last 100 years have been devoted to improving the art. One particular problem that has relevance to the instant invention is that the use of native or recombinant 'native' allergens for allergen-specific immunotherapy carries the risk of adverse allergic events. Though the allergens are divided into a plurality of COPs, the fragments may still retain IgE reactivity that would trigger an adverse event (See page

766). In the alternative, If IgE binding is successfully reduced by the COPs some potential problems are that the loss of IgE binding might reduce the uptake of allergen by tolerance-promoting dendritic cells that present FcεRI-bound IgE or competitive antibody classes of the same specificity might be less efficient in the absence of IgE specific epitopes. Therefore, the art recognizes that induction of desensitization and/ or tolerance to a specific allergen by any allergen-specific immunotherapy is highly unpredictable.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 55-65 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 55 and claims dependent thereupon, it is unclear how candidate COPs are screened for T cell stimulating activity and IgE binding without any contact or

detection steps. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized and a correlation step describing how the results of the assay allow for the determination. Claim 55 is missing contact and detection steps that would give an indication of how T cell stimulating activity and IgE binding are determined.

In claim 55, "the selected allergen" on line 6 lacks antecedent basis.

In claim 55, step 3b, 'IgE's' is indifinite because it is unclear why the " 's" possessive form of IgE is being recited.

In claim 56, 'the allergen holoprotein' lacks antecedent basis in claim 55 and the specification.

In claim 59, "said allergen" lacks antecedent basis in claim 55.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 55-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Kammerer et al. (Reference C9, IDS filed on 06/22/2004).

Kammerer et al. teach a method of mapping structural analysis was performed on the phopholipase A_2 (PL A_2) allergen to determine the T cell epitopes (In particular, Figure 1). 40-60 amino acid long overlapping peptides selected and used with particular emphasis as a potential immunotherapy (In particular, abstract). The long overlapping peptides overlapped one another at the separation sites by 10 residues to map the entire PL A_2 allergen (In particular, page 1017, left column last paragraph). The overlapping peptides were synthesized using a multi-peptide synthesizer (page 1017, left column, last paragraph). IgE binding to the long overlapping peptides was determined by immunoblotting and chemiluminescence (In particular, page 1018, 'Immunoblotting section; Figure 7 and page 1020, right column, second whole paragraph). T cell stimulation in response to the long overlapping peptides was determined and a mean stimulation index of >2 was determined to be a positive T cell response (In particular, page 1017, 'PBMC' proliferation assays section; page 1018, first

paragraph of results; and Figure 2). These long overlapping peptides stimulated T cell responses, but do not bind IgE in vitro, so they represent a valuable alternative to immunotherapy with native allergens (In particular, page 1024, last paragraph to page 1025). The reference suggests using in vivo intradermal tests to confirm that the peptides are useful for immunotherapy (page 1025, last paragraph).

The reference teachings anticipate the claimed invention.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 55 and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kammerer et al. in view of Spertini et al. (IDS filed on 07/26/2004).

Kammerer et al has been discussed supra.

The claimed invention differs from the prior art by the recitation of testing long overlapping peptides to confirm that the peptides are useful for immunotherapy by the

injection of COPs at a peptide concentration of .1 µg/ml or greater to induce a wheal and flare reaction less than or equal to 5mm.

Spertini et al. teaches the intradermal injection of three long (44-60 amino acid long) overlapping peptides at a peptide concentration of .1 µg/ml in 9 patients. Only 3 of the patients exhibited a positive reaction at day 70. The reference is silent as to what is defined as a positive reaction, but 6 of the 9 patients exhibited no reaction. Therefore, the wheal and flare reaction of 6 of the patients was less than 5mm in response to the 1 µg/ml intradermal injection.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Spertini et al. to those of Kemmerer et al. in order to measure the IgE binding activity of the long overlapping peptides in vivo data at a relevant concentration because in vivo data more reliably confirms the applicability of the long overlapping peptides for an effective immunotherapy technique. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

16. Claims 55 and 61- 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kammerer et al. in view of Shanti et al. (PTO-892, Page 2, Reference U).

Kemmerer et al. has been discussed supra.

The claims invention differs from the prior art by the recitation of using a dot blot to determine IgE binding activity.

Shanti et al. uses a dot-blot technique to determine IgE binding to Sa-II and tropomyosin shrimp allergen peptide fragments (page 5356, paragraph spanning left and right columns and Figure 1).

It would have been It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of Shanti et al. to the teachings of Kammerer et al. to determine IgE binding activity to overlapping peptide fragments using a dot blot assy.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because the dot blot as taught by Shanti et al. is a good way to test for IgE binding activity to allergen fragments (page 5356, paragraph spanning left and right columns, abstract, Figure 1). The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to

reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

February 2, 2007

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